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RESEARCH**

APPLICATION NUMBER:

21-143

CHEMISTRY REVIEW(S)

APR 18 2000

**DIVISION OF SPECIAL PATHOGENS AND IMMUNOLOGIC DRUG
PRODUCTS**

Review of Chemistry, Manufacturing, and Controls

NDA #: 21-143

CHEM.REVIEW #: 1

REVIEW DATE: 4/10/00

SUBMISSION/TYPE

DOCUMENT DATE

CDER DATE

ORIGINAL	6/16/99	6/17/99
Amendment (BC)	7/16/99	7/19/99
Amendment (BC)	12/20/99	12/21/99
Amendment (BC)	3/8/00	3/10/00
Amendment (BC)	3/31/00	4/03/00

NAME & ADDRESS OF APPLICANT:

Taro Pharmaceuticals Inc.
130 East Drive
Bramalea, Ontario, L6T1C3
Ph# (905) 791-8276

CONTACT:

Lorraine W. Sachs, RAC
Associate Director/Regulatory Affairs
5 Skyline Drive
Hawthorne, NY 10532
Ph # (914) 345-9001

DRUG PRODUCT NAME:

Proprietary: Trivagizole-3
Established: Clotrimazole Vaginal Cream, USP
Code #:

PHARMACOLOGICAL CATEGORY/INDICATION:

Treatment of vulvovaginal candidiasis.

DOSAGE FORM: Vaginal Cream

STRENGTHS: 2% cream, 100 mg per applicator

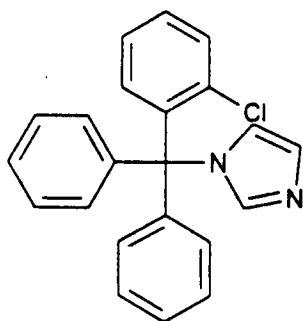
ROUTE OF ADMINISTRATION: Intravaginal

Rx/OTC: OTC

**CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA,
MOLECULAR WEIGHT:**

CAS-23593-75-1; $C_{22}H_{17}N_2Cl$; MW=344.85

1-(*o*-Chloro- α,α -diphenylbenzyl)imidazole



SUPPORTING DOCUMENTS:

NDA 20-574

RELATED DOCUMENTS: n/a

CONSULTS:

Trademark review (complete 2/8/00, satisfactory).

Site inspection (complete 3/20/00, satisfactory).

Environmental Assessment (categorical exclusion request acceptable).

Microbiology consult (complete 1/14/00, satisfactory).

REMARKS/COMMENTS:

This NDA submitted by Taro Pharmaceuticals, Inc. provides for clotrimazole vaginal cream, 2%, for the treatment of vulvovaginal candidiasis. The formulation of this product is very closely related to the previously approved cream of Schering-Plough HealthCare Products (SPHCP), Gyne-Lotrimin 3 Vaginal Cream (clotrimazole vaginal cream, 2%), NDA 20-574 (approved in November 1998), for which both, SPHCP and Taro, sponsored the clinical studies. In one of the two pivotal trials in those studies conducted by Taro and used to demonstrate the safety and efficacy, the formula of the product (clotrimazole vaginal cream, 2%) was the same as that marketed in Canada by Taro since 1989 and the one, which is a subject of the current NDA. SPHCP granted Taro the right of reference to all safety and efficacy data (including preclinical, toxicology and clinical data) provided in their NDA 20-574. Therefore the major portion of the current NDA 21-143 consists of CMC information that has been discussed in this review. Several faxes with questions

and comments were forwarded to Taro Pharmaceuticals, Inc. and were addressed by the applicant adequately. The comprehensive list of these questions and comments is provided in the end of this review. The trademark proposed by the applicant for this new product as Trivagizole-3 (clotrimazole vaginal cream) was found acceptable by the OPDRA. Copy of the OPDRA review is attached to this review.

CONCLUSIONS & RECOMMENDATIONS:

The NDA submission and amendments provide adequate information on the chemistry, manufacturing and controls for the production of Trivagizole-3 (clotrimazole vaginal cream). The related GMP and product specific inspections of the manufacturing facilities have been completed and found satisfactory. From the chemistry, manufacturing and controls viewpoint, the NDA is recommended for approval.

/S/

Dorota Matecka, Ph.D.
Review Chemist, HFD-590

/S/

Norman R. Schmuff, Ph.D.
Team Leader, HFD-590

4/18/2000

cc: Org. NDA 21-143
HFD-590/Division File
HFD-590/Team Leader/NSchmuff
HFD-830/DivDir/CChen
HFD-590/Chem/DMatecka
HFD-590/MO/JWinfield
HFD-590/Pharm/OMcMaster
HFD-590/Micro/LGosey
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District Office